REMARKS

Support for the amendments to claim 1 can be found in the Specification, for example, at pages 12-13; page 14, lines 8-11; and page 42, lines 9-14.

Comments Regarding Restriction Requirement

Applicants affirm the election, with traverse, of claims 1, 2, 13 and 14, corresponding to the invention of Group I. Applicants submit that, upon allowance of product claims 1, 2, 13 and 14, claims 6, 15 and 16, drawn to methods of making and use of the same, should be rejoined, per the Commissioner's Notice in the Official Gazette of March 26, 1996, entitled "Guidance on Treatment of Product and Process Claims in light of *In re Ochiai, In re Brouwer* and 35 U.S.C. § 103(b)" which sets forth the rules, upon allowance of product claims, for rejoinder of process claims covering the same scope of products.

Comments Regarding Priority Information

At the Examiner's suggestion, the first paragraph of the first page of the Specification has been amended to update the priority information regarding the parent application.

Comments Regarding Information Disclosure Statement

Initially, it is noted that the Examiner failed to completely examine Applicants' invention. Specifically, Applicants object to the Examiner's failure to obtain and fully consider the references cited in the parent application and listed on the Form 1449. According to M.P.E.P. § 609:

> ...the examiner ***will consider*** information which has been considered by the Office in a parent application when examining (A) a continuation application filed under 37 CFR 1.53(b) or filed under former 37 CFR 1.60, (B) a divisional application filed under 37 CFR 1.53(b) or filed under former 37 CFR 1.60, or (C) a continuation-in-part application (see MPEP Section 201.06(b)) filed under 37 CFR 1.53(b), and a list of the information need not be submitted in the continuation, divisional, or continuation-in-part application unless applicant desires the information to be printed on the patent. (Emphasis added)

As can be seen from the above, it is mandatory for the Examiner to consider information previously considered in a parent application. Although the Patent Office has facilities for obtaining copies of the cited information, References 2-5 and 7-10 of Applicants' form 1449 are nevertheless herein resubmitted. These references were originally submitted in the parent patent application Serial No. 09/131,648 filed August 10, 1998, now U.S. Patent Number 6,168,920, issued January 2, 2001. The Information Disclosure Statement and form 1449 for the parent patent application were mailed on November 4, 1998 and were received in the USPTO on November 9, 1998 (see attached copy of returned postcard indicating receipt of all ten references cited on form 1449). For this reason it is believed that no fee is necessary for resubmitting these references.

Comments Regarding Claim Objections

Claims 2 and 14 are objected to because they are dependent on rejected claim 1. It is believed that claim 1 is allowable. Therefore, this objection should be moot.

Indefiniteness Rejections under 35 U.S.C. § 112, Second Paragraph

Claims 1 and 13 are rejected under 35 U.S.C. § 112, second paragraph, as being allegedly indefinite. In particular, the Office Action asserts that:

> Claim 1 (13 dependent on) is indefinite in that it is vague in the recitation of the phrase "biologically active fragment" (June 4, 2002 Office Action at page 4)
>
> Claim 13 is indefinite in the recitation of "effective amount of a polypeptide" (June 4, 2002 Office Action at page 5)
>
> Claim 13 is indefinite in the recitation of "an acceptable excipient" (June 4, 2002 Office Action at page 5)

Claim 1 has been amended to remove the "biologically active fragment" language. Claim 13 has been amended to remove the recitation of "an effective amount" and "an acceptable excipient." Withdrawal of these objections is therefore requested.

Written Description Rejection under 35 U.S.C. § 112, First Paragraph

Claims 1 and 13 are rejected under 35 U.S.C. § 112, first paragraph, for alleged lack of an adequate written description. In particular, the Office Action asserts that:

> part b) of claim 1 is drawn to all possible polypeptides comprising a naturally occurring amino acid sequence at least 90% identical to an amino acid sequence of SEQ ID NO:1, wherein said protein has an undefined function/activity. (June 4, 2002 Office Action at page 6.)
>
> The genus of proteins that are claimed is a large variable genus with potentiality of comprising many functionally unrelated proteins. The specification also fails to describe additional representative species of these polypeptides by any identifying characteristics or properties other than the structural characteristics recited in claim 1, for which no predictability of function is apparent. (June 4, 2002 Office Action at page 7.)

This rejection is respectfully traversed.

The requirements necessary to fulfill the written description requirement of 35 U.S.C. 112, first paragraph, are well established by case law.

> . . . the applicant must also convey with reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was in possession *of the invention.* The invention is, for purposes of the "written description" inquiry, *whatever is now claimed. Vas-Cath, Inc. v. Mahurkar*, 19 USPQ2d 1111, 1117 (Fed. Cir. 1991)

Attention is also drawn to the Patent and Trademark Office's own "Guidelines for Examination of Patent Applications Under the 35 U.S.C. Sec. 112, para. 1", published January 5, 2001, which provide that :

> An applicant may also show that an invention is complete by disclosure of sufficiently detailed, relevant identifying characteristics[42] which provide evidence that applicant was in possession of the claimed invention,[43] i.e., complete or partial structure, other physical and/or chemical properties, functional characteristics when coupled with a known or disclosed correlation between function and structure, or some combination of such characteristics.[44] What is conventional or well known to one of ordinary skill in the art need not be disclosed in detail.[45] If a skilled artisan would have understood the inventor to be in possession of the claimed invention at the time of filing, even if every nuance of the claims is not explicitly described in the specification, then the adequate description requirement is met.[46]

Thus, the written description standard is fulfilled by both what is specifically disclosed and what is conventional or well known to one skilled in the art.

- **The specification provides an adequate written description of the claimed "variants" and "fragments" of SEQ ID NO:1**

The subject matter encompassed by claims 1 and 13 is either disclosed by the specification or is conventional or well known to one skilled in the art.

While not conceding the propriety of the Patent Office position, claim 1 has been revised to include the recitation of functional activity to define the claimed "variants", and the "fragment" language has been deleted. These amendments are made solely to expedite prosecution of the subject application. Applicants expressly do not disclaim equivalents which could include polypeptide variants of SEQ ID NO:1 having biological activities other than extracellular adhesion activity.

First note that the "variant" language of amended independent claim 1 recites an isolated polypeptide comprising "a naturally occurring amino acid sequence at least 90% identical to the amino acid sequence of SEQ ID NO:1, said naturally occurring amino acid sequence having extracellular adhesion activity." SEQ ID NO:1 is specifically disclosed in the application (see, for example, page 12, lines 24-31 and Figures 1A and 1B). Polypeptide variants having at least 90% identity to SEQ ID NO:1 are described, for example, at page 14, lines 8-11. Accordingly, the Specification provides an adequate written description of the recited polypeptide sequences.

One of ordinary skill in the art would recognize polypeptide sequences which are variants at least 90% identical to SEQ ID NO:1. Given any naturally occurring polypeptide sequence, it would be routine for one of skill in the art to recognize whether it was a variant of SEQ ID NO:1. Accordingly, the Specification provides an adequate written description of the recited variants of SEQ ID NO:1.

1. The present claims specifically define the claimed genus through the recitation of chemical structure

Court cases in which "DNA claims" have been at issue (which are hence relevant to claims to proteins encoded by the DNA) commonly emphasize that the recitation of structural features or chemical or physical properties are important factors to consider in a written description analysis of such

claims. For example, in *Fiers v. Revel*, 25 USPQ2d 1601, 1606 (Fed. Cir. 1993), the court stated that:

> If a conception of a DNA requires a precise definition, such as by structure, formula, chemical name or physical properties, as we have held, then a description also requires that degree of specificity.

In a number of instances in which claims to DNA have been found invalid, the courts have noted that the claims attempted to define the claimed DNA in terms of functional characteristics without any reference to structural features. As set forth by the court in *University of California v. Eli Lilly and Co.*, 43 USPQ2d 1398, 1406 (Fed. Cir. 1997):

> In claims to genetic material, however, a generic statement such as "vertebrate insulin cDNA" or "mammalian insulin cDNA," without more, is not an adequate written description of the genus because it does not distinguish the claimed genus from others, except by function.

Thus, the mere recitation of functional characteristics of a DNA, without the definition of structural features, has been a common basis by which courts have found invalid claims to DNA. For example, in *Lilly*, 43 USPQ2d at 1407, the court found invalid for violation of the written description requirement the following claim of U.S. Patent No. 4,652,525:

> 1. A recombinant plasmid replicable in procaryotic host containing within its nucleotide sequence a subsequence having the structure of the reverse transcript of an mRNA of a vertebrate, which mRNA encodes insulin.

In *Fiers*, 25 USPQ2d at 1603, the parties were in an interference involving the following count:

> A DNA which consists essentially of a DNA which codes for a human fibroblast interferon-beta polypeptide.

Party Revel in the *Fiers* case argued that its foreign priority application contained an adequate written description of the DNA of the count because that application mentioned a potential method for isolating the DNA. The Revel priority application, however, did not have a description of any particular DNA structure corresponding to the DNA of the count. The court therefore found that the Revel priority application lacked an adequate written description of the subject matter of the count.

Thus, in *Lilly* and *Fiers*, nucleic acids were defined on the basis of functional characteristics and were found not to comply with the written description requirement of 35 U.S.C. § 112; *i.e.*, "an mRNA of a vertebrate, which mRNA encodes insulin" in *Lilly*, and "DNA which codes for a human fibroblast interferon-beta polypeptide" in *Fiers*. In contrast to the situation in *Lilly* and *Fiers*, the claims at issue in the present application define polypeptides in terms of chemical structure, rather than functional characteristics. For example, the language of amended independent claim 1 recites chemical structure to define the claimed genus:

1. (Once amended.) An isolated polypeptide selected from the group consisting of:
a) a polypeptide comprising the amino acid sequence of SEQ ID NO:1, and
b) a polypeptide comprising a naturally occurring amino acid sequence at least 90% identical to the amino acid sequence of SEQ ID NO:1, said naturally occurring amino acid sequence having extracellular adhesion activity.

From the above it should be apparent that the claims of the subject application are fundamentally different from those found invalid in *Lilly* and *Fiers*. The subject matter of the present claims is defined in terms of the chemical structure of SEQ ID NO:1. In the present case, there is no reliance only on a description of functional characteristics of the claimed polypeptides. The polypeptides defined by the claims of the present application recite structural features, and cases such as *Lilly* and *Fiers* stress that the recitation of structure is an important factor to consider in a written description analysis of claims of this type. By failing to base its written description inquiry "on whatever is now claimed," the Examiner failed to provide an appropriate analysis of the present claims and how they differ from those found not to satisfy the written description requirement in *Lilly* and *Fiers*.

2. The present claims do not define a genus which is "highly variant"

Furthermore, the claims at issue do not describe a genus which could be characterized as "highly variant". Available evidence illustrates that, rather than being a large variable genus, the claimed genus is of narrow scope.

In support of this assertion, the Examiner's attention is directed to the reference by Brenner et al. ("Assessing sequence comparison methods with reliable structurally identified distant evolutionary relationships," Proc. Natl. Acad. Sci. USA (1998) 95:6073-6078)(Reference No. 1). Through exhaustive analysis of a data set of proteins with known structural and functional relationships and with <90% overall sequence identity, Brenner et al. have determined that 30% identity is a reliable threshold for establishing evolutionary homology between two sequences aligned over at least 150 residues (Brenner et al., pages 6073 and 6076). Furthermore, local identity is particularly important in this case for assessing the significance of the alignments, as Brenner et al. further report that ≥40% identity over at least 70 residues is reliable in signifying homology between proteins (Brenner et al., page 6076).

The present application is directed, *inter alia*, to polypeptides related to human prostate carcinoma tumor antigen-1 (PCTA-1), a member of the galectin class of proteins. In particular, the polypeptides are selected from polypeptides comprising SEQ ID NO:1, and polypeptides comprising naturally occurring amino acid sequences at least 90% identical to SEQ ID NO:1 and having extracellular adhesion activity. In accordance with Brenner et al., naturally occurring molecules may exist which could be characterized as human prostate carcinoma tumor antigen-1 or proteins belonging to the galectin class of proteins and which have as little as 30% identity over at least 150 residues to SEQ ID NO:1. The "variant language" of the present claims recites a polypeptide comprising "a naturally occurring amino acid sequence at least 90% identical to the amino acid sequence of SEQ ID NO:1, said naturally occurring amino acid sequence having extracellular adhesion activity" (note that SEQ ID NO:1 has 336 amino acid residues). This variation is far less than that of all potential galectin proteins related to SEQ ID NO:1, i.e., those galectin proteins having as little as 30% identity over at least 150 residues to SEQ ID NO:1.

3. The state of the art at the time of the present invention is further advanced than at the time of the *Lilly* and *Fiers* applications

In the *Lilly* case, claims of U.S. Patent No. 4,652,525 were found invalid for failing to comply with the written description requirement of 35 U.S.C. § 112. The '525 patent claimed the benefit of priority of two applications, Application Serial No. 801,343 filed May 27, 1977, and Application Serial

No. 805,023 filed June 9, 1977. In the *Fiers* case, party Revel claimed the benefit of priority of an Israeli application filed on November 21, 1979. Thus, the written description inquiry in those cases was based on the state of the art at essentially the "dark ages" of recombinant DNA technology.

The present application has a priority date of August 10, 1998. Much has happened in the development of recombinant DNA technology in the 18 or so years from the time of filing of the applications involved in *Lilly* and *Fiers* and the present application. For example, the technique of polymerase chain reaction (PCR) was invented. Highly efficient cloning and DNA sequencing technology has been developed. Large databases of protein and nucleotide sequences have been compiled. Much of the raw material of the human and other genomes has been sequenced. With these remarkable advances, one of skill in the art would recognize that, given the sequence information of SEQ ID NO:1, and the additional extensive detail provided by the subject application, the present inventors were in possession of the claimed polypeptide variants at the time of filing of this application.

4. Summary

The Office Action failed to base its written description inquiry "on whatever is now claimed." Consequently, the Action did not provide an appropriate analysis of the present claims and how they differ from those found not to satisfy the written description requirement in cases such as *Lilly* and *Fiers*. In particular, the claims of the subject application are fundamentally different from those found invalid in *Lilly* and *Fiers*. The subject matter of the present claims is defined in terms of the chemical structure of SEQ ID NO:1. The courts have stressed that structural features are important factors to consider in a written description analysis of claims to nucleic acids and proteins. In addition, the genus of polypeptides defined by the present claims is adequately described, as evidenced by Brenner et al. Furthermore, there have been remarkable advances in the state of the art since the *Lilly* and *Fiers* cases, and these advances were given no consideration whatsoever in the position set forth by the Office Action.

For at least the above reasons it is believed that claims 1 and 13 meet the written description requirement of 35 U.S.C. § 112, first paragraph. It is therefore requested that this rejection be withdrawn.

Enablement Rejections under 35 U.S.C. § 112, First Paragraph

Claims 1 and 13 are rejected under 35 U.S.C. § 112, first paragraph, allegedly for lacking an enabling disclosure with respect to variants and biologically active fragments of SEQ ID NO:1. The Examiner has specifically stated that "[t]he specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims." (June 4, 2002 Office Action at page 8.) The Examiner further states "applicants have not provided sufficient guidance to enable one of ordinary skill in the art to use the claimed invention in a manner reasonably correlated with the scope of the claims broadly including all possible polypeptides comprising a naturally occurring amino acid sequence at least 90% identical to an amino acid sequence of SEQ ID NO:3, [sic] and fragments of SEQ ID NO:1, wherein said polypeptide has an undefined function activity." (June 4, 2002 Office Action at page 9.) These rejections are respectfully traversed.

While not conceding the propriety of the Patent Office position, claim 1 has been revised to include the recitation of functional activity to define the claimed "variants", and the "fragment" language has been deleted. These amendments are made solely to expedite prosecution of the subject application. Applicants expressly do not disclaim equivalents which could include polypeptide variants of SEQ ID NO:1 having biological activities other than extracellular adhesion activity.

For at least the above reasons, withdrawal of the enablement rejection under 35 U.S.C. § 112, first paragraph, is requested.

Prior Art Rejections under 35 U.S.C. § 102(b)

Claims 1 and 13 are rejected under 35 U.S.C. § 102(b) for alleged anticipation by Ni et al. (WO 98/31799) or Su et al. (Proc. Natl. Acad. Sci. USA Vol 93, pp. 7252-7257, July 1996). In particular, the Office Action asserts that claims 1 and 13 are anticipated by Ni et al. due to a description of a 133 amino acid polypeptide that is 100% identical to amino acid residues 204 to 336 of SEQ ID NO:1, and that the therapeutically effective amounts of said polypeptide and a pharmaceutically acceptable carrier or excipient taught by Ni et al. allegedly anticipates claim 13 of the instant application. Further, the Office Action asserts that Su et al. allegedly anticipates biologically active and

immunogenic fragments of SEQ ID NO:1 and compositions of same and an excipient because it teaches an 8 amino acid fragment with 100% identity to amino acids 93-100 of SEQ ID NO:1. These rejections are respectfully traversed.

Amended independent claim 1 recites:

1. An isolated polypeptide selected from the group consisting of:
a) a polypeptide comprising the amino acid sequence of SEQ ID NO:1, and
b) a polypeptide comprising a naturally occurring amino acid sequence at least 90% identical to the amino acid sequence of SEQ ID NO:1, said naturally occurring amino acid sequence having extracellular adhesion activity.

While not conceding the propriety of the Patent Office position, claim 1 has been revised to include the recitation of functional activity to define the claimed "variants", and the "fragment" language has been deleted. These amendments are made solely to expedite prosecution of the subject application. Neither Ni et al. nor Su et al. provides any recognition of any polypeptide that is recited in amended claim 1 or of compositions as recited in amended claim 13. Applicants expressly do not disclaim equivalents which could include polypeptide variants of SEQ ID NO:1 having biological activities other than extracellular adhesion activity.

For at least the above reasons, it is requested that the § 102 rejections be withdrawn.

CONCLUSION

In light of the above amendments and remarks, Applicants submit that the present application is fully in condition for allowance, and request that the Examiner withdraw the outstanding rejections. Early notice to that effect is earnestly solicited.

If the Examiner contemplates other action, or if a telephone conference would expedite allowance of the claims, Applicants invite the Examiner to contact Applicants' Attorney at (650) 855-0555.

Applicants believe that no fee is due with this communication. However, if the USPTO determines that a fee is due, the Commissioner is hereby authorized to charge Deposit Account No. **09-0108.**

Respectfully submitted,

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VERSION WITH MARKINGS TO SHOW CHANGES MADE

IN THE SPECIFICATION:

The paragraph beginning at line 2 of page 1 has been amended as follows:

This application is a divisional application of U.S. application serial number 09/131,648, filed August 10, 1998, now U.S. Patent No. 6,168,920, entitled EXTRACELLULAR ADHESIVE PROTEINS, issued January 2, 2001, all of which applications and patents are hereby incorporated herein by reference.

IN THE CLAIMS:

Claims 3-5, 7-12 and 17-20 have been cancelled.

Claims 1, 2, 13 and 14 have been amended as follows:

1. (Once amended.) An isolated polypeptide [comprising an amino acid sequence] selected from the group consisting of:

a) a polypeptide comprising the [an] amino acid sequence of SEQ ID NO:1, and

b) a polypeptide comprising a naturally occurring amino acid sequence [having] at least 90% [sequence identity] identical to [an] the amino acid sequence of SEQ ID NO:1, said naturally occurring amino acid sequence having extracellular adhesion activity

[c) a biologically active fragment of an amino acid sequence of SEQ ID NO:1, and

d) an immunogenic fragment of an amino acid sequence of SEQ ID NO:1].

2. (Once amended.) An isolated polypeptide of claim 1, [having a] comprising the sequence of SEQ ID NO:1.

13. (Once amended.) A composition comprising [an effective amount of] a polypeptide of claim 1 and an [acceptable] excipient.

14. (Once amended.) A composition of claim 13, wherein the polypeptide [has] comprises the sequence of SEQ ID NO:1.